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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/929,770	08/14/2001	Napoleone Ferrara	479.58-6	9615

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EXAMINER	
SPECTOR, LORRAINE	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 12/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/929,770	FERRARA ET AL.	
	Examiner	Art Unit	
	Lorraine Spector, Ph.D.	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 August 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *45-79* is/are pending in the application.

4a) Of the above claim(s) *56,57 and 68-79* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *45-55 and 58-67* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *45-79* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-44 have been cancelled. Claims 45-79 are newly submitted.

Any rejection not expressly maintained or presented herein has been withdrawn in view of applicants amendments to the claims.

The double patenting rejection over the claims of application 08/473276 is withdrawn, as the current claims are restricted to bovine VEGF, and the copending claims are restricted to human VEGF.

Newly introduced claims 61 and 64-68 are in a product-by-process format. The purification or production of a protein by a particular process does not impart novelty or unobviousness to a protein when the same protein is taught by the prior art. This is particularly true when the properties of the protein are not changed by the process in an unexpected manner. See In re Thorpe, 227 USPQ 964 (CAFC 1985); In re Marosi, 218 USPQ 289, 292-293 (CAFC 1983); In re Brown, 173 USPQ 685 (CCPA 1972). Therefore, even if a particular process used to prepare a protein is novel and unobvious over the prior art, the protein per se, even when limited to the particular process, is unpatentable over the same protein taught by the prior art. See In re King, 107 F.2d 618, 620, 43 U.S.P.Q. 400, 402 (C.C.P.A. 1939); In re Merz, 97 F.2d 599, 601, 38 U.S.P.Q. 143, 144-45 (C.C.P.A. 1938); In re Bergy, 563 F.2d 1031, 1035, 195 U.S.P.Q. 344, 348 (C.C.P.A. 1977) vacated 438 U.S. 902 (1978); and United States v. Ciba-Geigy Corp., 508 F. Supp. 1157, 1171, 211 U.S.P.Q. 529, 543 (D.N.J. 1979). As none of the recited processes would result in a particular degree of purity, nor affect the composition of the resultant protein, such limitations are given only minimal weight in considering the prior art. With respect to issues under 35 U.S.C. §112, first paragraph, all claim limitations must be considered.

Claims 56, 57 and 68-73 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 12/29/2003.

Claims 74-79 are hybrid claims, being drawn to the pharmaceutical composition used in the method of the claims from which they depend. As such claims would not be properly dependent if interpreted to be composition claims, as a composition does not further limit a method (they are distinct categories of invention), the claims are interpreted as limiting the composition being used in the method. As such, they are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 12/29/2003.

Newly introduced claims 45-55 and 58-67 are under consideration.

Terminal Disclaimer

The terminal disclaimer filed on 8/23/2004 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of 08/473276 has been reviewed and is accepted. The terminal disclaimer has been recorded.

Specification

The disclosure is objected to because of the following informalities:

The amendment filed 8/23/2004 is objected to because it is not clear whether the statement that "the common text" of the parent applications is incorporated by reference refers to the text that the various parents have in common with each other, or that which each has in common with the instant application. If the former is the case, such would still be subject to a new matter rejection. If the latter is the case, the incorporation would not be improper, but would serve no purpose.

Appropriate correction is required.

Claim Objections

Applicant is advised that should claims 45 and 47 be found allowable, claims 48 and 49, respectively, will be objected to under 37 CFR 1.75 as being substantial duplicates thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 51, 55, 58-60, 62 and 63 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 51 is indefinite as it is not clear what is meant by "-.[1]". Deletion of the period (".") would be remedial.

Claims 55, and 58 are indefinite for using the definite article "the", rather than an indefinite article such as "an" at the beginning of the claims. As there could be innumerable pharmaceutical compositions comprising the claimed protein, it is not clear to which one the article "the" refers.

Claim 55 is also indefinite as it is not clear how the human being is being used. Further, it is not clear how the recitation of intended use further limits the pharmaceutical composition of claim 48. In this latter regard, claims 62 and 63 are similarly indefinite.

Claim 60 is indefinite because a pharmaceutical composition is not further limited by the dosage at which it is used, and because dosage is not an adaptation for wound healing.

The remaining claim(s) are rejected for depending from an indefinite claim.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 64-67 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Newly introduced claims 64-67 are product-by-process claims requiring the recombinant expression of the claimed growth factor

The claims require the recombinant DNA production of the claimed protein. That would entail having the DNA encoding said protein, and expressing such in an appropriate host cell system. The nucleic acid sequences necessary for such recombinant production are not disclosed in the specification as originally filed. Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116).

Simply put, the claims require a full-length, functional nucleic acid sequence encoding folliculo-stellate derived growth factor, whereas the specification provides only a very small portion of the amino acid sequence of the bovine protein, and does not provide any nucleic acid sequence from any species. The specification merely provides an invitation to find the nucleic acid, and does not provide any evidence of possession of such nucleic acids. The skilled artisan cannot envision the detailed chemical structure of the polynucleotides required for the process recited in the rejected claims, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and

reference to a potential method of isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601 at 1606 (CAFC 1993) and Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016.

One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 1481 at 1483. In Fiddes, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence. In this case only a partial amino acid sequence is provided. No complete amino acid sequence is provided, and no nucleic acids are provided.

Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Therefore, as the specification fails to describe the nucleic acids required to carry out the process recited in the claims, the claims fail to meet the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Applicants traversal that is would not require undue experimentation to obtain the required DNA has been fully considered but is not deemed persuasive. Such *might* be the case if the *entire* amino acid sequence of the protein had been disclosed. However, it has not. What is disclosed is a partial sequence, and an invitation to experiment. Such does not fulfill the written description requirement of 35 U.S.C. §112, first paragraph. Applicant is again reminded that Vas-Cath makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claims 64-67 19, 20 and 40 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, for reasons of record as applied to claims 19, 20 and 40 in the previous Office Action.

Applicants traversal at page 16 of the response filed 8/18/2004 has been fully considered but is not deemed persuasive. Applicants argue that undue experimentation would not be

required, but provide no fact or evidence in support of the argument. Accordingly, such is not persuasive.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103.

Claims 45-55 and 58-67 are rejected under 35 U.S.C. § 103 as being unpatentable over Connolly et al. (U.S. Pat. No. 5,008,196, cited by applicants) or Senger (Science, 219, 983-985, 1983, cited by applicants) or Dvorak (U.S. Pat. No. 4,456,550, cited by applicants) or Criscuolo et al (J. Neurosurg. 69, 254-262, 1988, cited by applicants), any one of the aforementioned in view of Chen et al. (U.S. Pat. No. 5,073,492, cited by applicants) for reasons of record as applied to Claims 1-3, 11, 14-16, 18-25, 29-32, 34-37 and 40 in the previous office action.

The teachings of the primary references are discussed above. Each teaches isolation of VEGF from one or more animal species. However, none discloses bovine VEGF. '492 teaches the partial purification of bovine VEGF approximately the same size as guinea pig VPF (VEGF; Fig. 2, fraction III) which selectively stimulates endothelial cell growth (Fig. 5 and col. 4, line 6

to col. 5, line 6). Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to use the method of any one of the primary references to purify bovine VEGF because '492 discloses that VEGF is present in bovine tissues. One would have been motivated to make this modification in order to have bovine VEGF for use in veterinary applications for cattle. The recited amino acid sequences and molecular weights are inherent to bovine VEGF. Accordingly, the invention, taken as a whole, is *prima facie* obvious over the prior art.

Applicants traversal that the rejection is overcome by the newly presented claims is not persuasive.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 45-55 and 58-67 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 26-35 of copending

Application No. 10/177485. Although the conflicting claims are not identical, they are not patentably distinct from each other because each is drawn to VEGF, including bovine VEGF, and compositions thereof.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 45-55 and 58-67 are provisionally rejected under 35 U.S.C. 103(a) as being obvious over copending Application No. 10/177485 which has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the copending application, it would constitute prior art under 35 U.S.C. 102(e) if published or patented. This provisional rejection under 35 U.S.C. 103(a) is based upon a presumption of future publication or patenting of the conflicting application.

This provisional rejection might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the copending application was derived from the inventor of this application and is thus not the invention "by another," or by a showing of a date of invention for the instant application prior to the effective U.S. filing date of the copending application under 37 CFR 1.131. For applications filed on or after November 29, 1999, this rejection might also be overcome by showing that the subject matter of the reference and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person. See MPEP § 706.02(l)(1) and § 706.02(l)(2).

Claims 45-55 and 58-67 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 32-35 and 41 of copending Application No. 10/155492. Although the conflicting claims are not identical, they are not patentably distinct from each other because each is drawn to VEGF, including bovine VEGF, and compositions thereof.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 45-55 and 58-67 are provisionally rejected under 35 U.S.C. 103(a) as being obvious over copending Application No. 10/155492 which has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the copending application,

it would constitute prior art under 35 U.S.C. 102(e) if published or patented. This provisional rejection under 35 U.S.C. 103(a) is based upon a presumption of future publication or patenting of the conflicting application.

This provisional rejection might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the copending application was derived from the inventor of this application and is thus not the invention "by another," or by a showing of a date of invention for the instant application prior to the effective U.S. filing date of the copending application under 37 CFR 1.131. For applications filed on or after November 29, 1999, this rejection might also be overcome by showing that the subject matter of the reference and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person. See MPEP § 706.02(l)(1) and § 706.02(l)(2).

Claims 45-55 and 58-67 are rejected under 35 U.S.C. 102(f) as there is evidence that applicants are not the inventors of the claimed subject matter. See US Patent Application numbers 10/1558492 and 10/177485. It is noted that the applications have been published as US 2003 3011437 and 2003 0108989, respectively.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37

CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

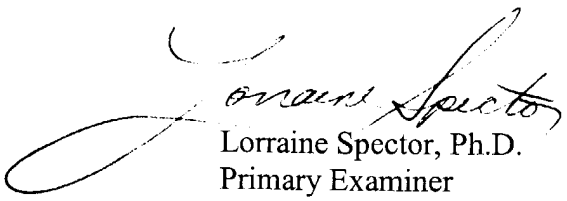
Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Lorraine M. Spector. Dr. Spector can normally be reached Monday through Friday, 9:00 A.M. to 3:00 P.M. ***Effective 1/21/2004, Dr. Spector's telephone number is 571-272-0893.***

If attempts to reach the Examiner by telephone are unsuccessful, please contact the Examiner's supervisor, Ms. Brenda Brumback, at telephone number 571-272-0961.

Certain papers related to this application may be submitted to Technology Center 1600 by facsimile transmission The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). NOTE: If Applicant does submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Official papers filed by fax should be directed to 571-273-8300. Faxed draft or informal communications with the examiner should be directed to ***571-273-0893.***

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Lorraine Spector, Ph.D.
Primary Examiner

12/20/2004